Administration of Engerix B on a Schedule with Intervals Longer than 0, 1 and 6 Months.

This information is provided in response to your request for information regarding Engerix B® (hepatitis B vaccine).

SUMMARY

- GlaxoSmithKline (GSK) does not make recommendations regarding the administration of hepatitis B vaccine recombinant at longer than the recommended dosing intervals. GSK can offer recommendations based only on the approved dosing schedules in the local label for hepatitis B vaccine recombinant. Please see the local label for all approved dosing schedules.
- In an open-label, randomised study, 98% of children (5 through 16 years of age, N = 389) achieved seroprotective antibody titres (antibodies to hepatitis B surface antigen ≥10 mIU/mL) after receiving 3 doses of hepatitis B vaccine recombinant on a 0, 12, and 24 month schedule. However, when compared to the antibody response in children randomised to receive hepatitis B vaccine recombinant on a 0, 1 and 6 month schedule, geometric mean titres were significantly lower (3158.7 mIU/mL compared to 5687.4 mIU/mL, $P = 0.02$).
- In a non-controlled study, adolescents and young adults (mean age = 16 years) were given a dose of hepatitis B vaccine recombinant and instructed to return for doses at 1 and 6 months later. However, some returned more than 1 month late for the second (n = 62) or third (n = 42) doses. Based on logistic regression models, delaying the second or third doses did not affect seroprotection rates.
- Adverse event data were not reported in these studies.
- The Advisory Committee on Immunization Practices (ACIP) to the Centers for Disease Control and Prevention (CDC) has issued recommendations on the administration of vaccines at longer than the recommended intervals.

GlaxoSmithKline (GSK) does not make recommendations regarding the administration of hepatitis B vaccine recombinant at longer than the recommended dosing intervals. GSK can offer recommendations based only on the approved dosing schedules in the local label for hepatitis B vaccine recombinant. Please see the local label for all approved dosing schedules.

CLINICAL STUDIES

Study in Children and Adolescents (United States)

An open-label, randomised trial, involving 389 healthy children and adolescents (5 through 16 years of age), compared the antibody response to hepatitis B vaccine recombinant 10 mcg IM on a 0, 1 and 6 month (n = 181) schedule to a 0, 12 and 24 month (n = 161) dosing schedule.[1] Table 1 summarises the seroprotection and geometric mean titre (GMT) results before and after the third dose of each series. Safety data were not reported.

Table 1. Antibody Response to Hepatitis B Vaccine Recombinant 10 mcg Administered on a 0, 1 and 6 or 0, 12 and 24 Month Dosing Schedule[1]

Outcome	Dosing Schedule	
	0, 1 and 6 Months (N = 181)	0, 12 and 24 Months (N = 161)
SP Rate (%) immediately prior to third dose	92.3	88.8
GMT (mIU/mL) immediately prior to third dose	117.9	162.1
SP Rate (%) 1 month after third dose	99.5	98.1
GMT (mIU/mL) 1 month after third dose	5687.4*	3158.7
GMT = Geometric mean titre; N = Number of vaccinees; SP = Seroprotection (antibodies to hepatitis B surface antigen titre ≥10 mIU/mL) *P = 0.02 compared to the 0, 12 and 24 month schedule		

Study in Adolescents and Young Adults (United States)

A non-controlled study evaluated the immunogenicity of delaying the second or third dose of hepatitis B vaccine recombinant 20 mcg in adolescents and young adults (mean age: 16 years).[2] Each participant in the study was administered a first dose of hepatitis B vaccine recombinant and informed to return for doses at 1 and 6 months; however, varying schedules occurred according to their natural adherence patterns. In Group 1 (n = 150), the elapsed time between the first and second doses ranged from 1 to 11 months. In Group 2 (n = 115), the elapsed time between the first and third dose ranged from 5 to 16 months (the second dose was administered within 2 months of the first dose). Seroprotection rates (anti-HBs ≥10 mIU/mL) were not affected by late vaccinations according to logistic regression models. The GMTs after the second dose of hepatitis B vaccine recombinant in Group 1 and the third dose in Group 2 are shown in Table 2 and Table 3, respectively. Safety data were not reported.

Table 2. GMTs After Varying Times Between First and Second Doses*[2]

Time From First to Second Immunisation	N	GMT (mIU/mL)
1 to 2 Months	88	33.3
3 to 5 Months	21	60.8
6 to 11 Months	41	203.4
GMT = Geometric mean titre; N = Number of vaccinees *All second immunisations were completed at least 3 months before the first titre follow-up visit		

Table 3. GMTs After Varying Times Between First and Third Doses*[2]

Time From First to Third Immunisation	N	GMT (mIU/mL)
5 to 7 Months	73	966.9
8 to 10 Months	14	1401.7
11 to 16 Months	28	4438.1
GMT = Geometric mean titre; N = Number of vaccinees *In all vaccinees the second immunisation was within 2 months of the first immunisation, and the third immunisation was at least 3 months before the second titre follow-up visit		

THE ADVISORY COMMITTEE ON IMMUNIZATION PRACTICES (ACIP) TO THE CENTERS FOR DISEASE CONTROL AND PREVENTION (CDC) RECOMMENDATIONS

The Advisory Committee on Immunization Practices (ACIP) to the Centers for Disease Control and Prevention (CDC) has issued the following recommendations on the administration of vaccines at longer than the recommended intervals:[3] "Vaccination providers should administer vaccines as close to the recommended intervals as possible. However, longer-than-recommended intervals between doses do not reduce final antibody concentrations, although protection might not be attained until the recommended number of doses has been administered. An interruption in the vaccination schedule does not require restarting the entire series of a vaccine or toxoid or addition of extra doses."

Some information contained in this response may not be included in the approved GlaxoSmithKline Local Label. This response is not intended to offer recommendations for administering this product in a manner inconsistent with its approved labelling.

Adverse events should be reported. Reporting forms and information can be found at *www.yellowcard.gov.uk*. Adverse events should also be reported to GlaxoSmithKline on 0800 221 441.

If you become aware of patients who have received this product at any time during their pregnancy, we encourage healthcare professionals to report such information to the company.

This response was developed according to the principles of evidence-based medicine and therefore references may not be all-inclusive.

REFERENCE(S)

1. Halsey NA, Moulton LH, O'Donovan JC, et al. Hepatitis B vaccine administered to children and adolescents at yearly intervals. Pediatrics 1999;103:1243-1247.*
2. Middleman AB, Kozinetz CA, Robertson LM, et al. The effect of late doses on the achievement of seroprotection and antibody titer levels with hepatitis B immunization among adolescents. Pediatrics 2001;107:1065-1069.*
3. Centers for Disease Control and Prevention. General recommendations on immunization. Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 2011;60(No.2):1-64.*